AMENDMENTS TO THE CLAIMS

Claims 3, 8-12, 15, 18-23, 25-29, and 34 are currently pending. Please amend claims 3 and 15, as indicated below. This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing Of Claims

- 1-2. (Canceled)
- 3. (Currently amended) A compound of the formula:

$$Q_{3} \xrightarrow{R} Y \xrightarrow{R} Y \xrightarrow{Q_{2}} Q_{3} \xrightarrow{R} Y \xrightarrow{R} Y \xrightarrow{R} Q_{2}$$

$$O \xrightarrow{NH_{2}} N \xrightarrow{R} Q_{2}$$

$$O \xrightarrow{NH_{2}} N \xrightarrow{NH_{2}} Q_{2}$$

$$O \xrightarrow{NH_{2}} (Ie) \qquad Or \qquad (Ig)$$

wherein:

Q₃ is a 5-6 membered aromatic carbocyclic or heterocyclic ring system; or an 8-10 membered bicyclic ring system—comprising consisting of aromatic carbocyclic rings, aromatic heterocyclic rings or a combination of an aromatic carbocyclic ring and an aromatic heterocyclic ring; wherein Q₃ is substituted with 1 to 4 substituents, each of which is independently selected from halo; C₁-C₃ alkyl optionally substituted with NR'₂, OR', CO₂R' or CONR'₂; O-(C₁-C₃)-alkyl optionally substituted with NR'₂, OR', CO₂R' or CONR'₂; NR'₂; OCF₃; CF₃; NO₂; CO₂R'; CONHR'; SR'; S(O₂)N(R')₂; SCF₃; CN; N(R')C(O)R⁴; N(R')C(O)OR⁴; N(R')C(O)C(O)R⁴; N(R')S(O₂)R⁴; N(R')R⁴; N(R⁴)₂; OR⁴; OC(O)R⁴; OP(O)₃H₂; or N=CH-N(R')₂;

 Q_2 is selected from 5-6 membered aromatic carbocyclic or heterocyclic ring systems, or 8-10 membered bicyclic ring systems consisting of aromatic carbocyclic rings, aromatic heterocyclic rings or a combination of an aromatic carbocyclic ring and an aromatic heterocyclic ring; wherein:

Q₂ is optionally substituted with up to 4 substituents, independently selected from halo, CH=N-OH, or CH=O; C₁-C₃ straight or branched alkyl optionally substituted with NR'₂, OR', CO₂R', S(O₂)N(R')₂, N=CH-N(R')₂, R³, NH-CH₃, NHCH₂CH₂OH, NHCH₂CH(OH)CH₂OH, CH₂OCH₂OCH₃, NHCH₂CH₂NH₂, NH-phenyl, piperazinyl, pyrrolidinyl or CONR'₂; O-(C₁-C₃)-alkyl optionally substituted with NR'₂, OR', CO₂R', S(O₂)N(R')₂, N=CH-N(R')₂, R³, or CONR'₂; NR'₂; OCF₃; CF₃; NO₂; CO₂R'; CONHR'; R³; OR³; NHR³; SR³; C(O)R³; C(O)N(R')R³; C(O)OR³; SR'; S(O₂)N(R')₂; SCF₃; N=CH-N(R')₂; CH=N-OH; CH=O; or CN;

wherein R' is selected from hydrogen, (C₁-C₃)-alkyl; (C₂-C₃)-alkenyl or alkynyl; phenyl or phenyl substituted with 1 to 3 substituents independently selected from halo, methoxy, cyano, nitro, amino, hydroxy, methyl or ethyl;

R³ is selected from a 5-6 membered aromatic carbocyclic or heterocyclic ring system;

 R^4 is $(C_1$ - $C_4)$ -alkyl optionally substituted with $N(R')_2$, OR', CO_2R' , $CON(R')_2$, or $SO_2N(R^2)_2$; or a 5-6 membered carbocyclic or heterocyclic ring system optionally substituted with $N(R')_2$, OR', CO_2R' , $CON(R')_2$, or $SO_2N(R^2)_2$;

$$X \text{ is selected from -S-, -O-, -S(O_2)-, -S(O)-, -N(R^2)-, -N(R^2)-S(O_2)-,} \\ -N(R^2)-C(O)O-, -O-C(O)-N(R^2), -C(O)-, -C(O)O-, -O-C(O)-, -C(O)-N(R^2)-, -N(R^2)-C(O)-,} \\ -C(R^2)_2-, -C(OR^2)_2-, -CH(OH)-;$$

each R is independently selected from hydrogen, $-R^2$, $-N(R^2)_2$, $-OR^2$, SR^2 , $-C(O)-N(R^2)_2$, $-S(O_2)-N(R^2)_2$, or $-C(O)-OR^2$, wherein two adjacent R are optionally bound to one another and, together with each carbon to which they are respectively bound, form a 4-8 membered carbocyclic or heterocyclic ring;

 R^2 is selected from hydrogen, (C_1-C_3) -alkyl, or (C_2-C_3) -alkenyl; each optionally substituted with $-N(R')_2$, -OR', SR', $-C(O)-N(R')_2$, $-S(O_2)-N(R')_2$, -C(O)-OR', or R^3 ;

Y is C;

A, if present, is CR'; and

n is 1;

provided that when a compound is of formula Ig, Q_3 is 2,6-dichlorophenyl and both R substituents are H, then Q_2 is neither phenyl nor p-fluorophenyl; and

when a compound is of formula Ie, and Q_3 is 2,6-dichlorophenyl, both R substituents are H, and X is S, then Q_2 is not phenyl.

4-7. (Canceled)

8. (Previously presented) The compound according to claim 3, wherein Q_2 is selected from phenyl or pyridyl and wherein Q_2 optionally contains up to 3 substituents, each of which is independently selected from chloro, fluoro, bromo, methyl, ethyl, isopropyl, -

 OCH_3 , -OH, $-NH_2$, $-CF_3$, $-OCF_3$, $-SCH_3$, $-OCH_3$, -C(O)OH, $-C(O)OCH_3$, $-CH_2NH_2$, $-N(CH_3)_2$, $-CH_2$ -pyrrolidine and $-CH_2OH$.

9. (Previously presented) The compound according to claim 8, wherein, Q_2 is selected from:

unsubstituted 2-pyridyl or unsubstituted phenyl.

- $10. \qquad (Previously\ presented)\ \ The\ compound\ according\ to\ claim\ 9,\ wherein\ Q_2$ is selected from phenyl, 2-isopropylphenyl, 3,4-dimethylphenyl, 2-ethylphenyl,
- 3-fluorophenyl, 2-methylphenyl, 3-chloro-4-fluorophenyl, 3-chlorophenyl,
- 2-carbomethoxylphenyl, 2-carboxyphenyl, 2-methyl-4-chlorophenyl, 2-bromophenyl,

2-pyridyl, 2-methylenehydroxyphenyl, 4-fluorophenyl, 2-methyl-4-fluorophenyl,

- 2-chloro-4-fluorophenyl, 2,4-difluorophenyl, 2-hydroxy-4-fluorophenyl or
- 2-methylenehydroxy-4-fluorophenyl.
- 11. (Previously presented) The compound according to claim 3, wherein X is selected from –S-, -O-, -S(O₂)-, -S(O)-, -N(R²)-, -C(R²)₂- or –C(O)-.
- 12. (Previously presented) The compound according to claim 11, wherein \boldsymbol{X} is \boldsymbol{S} .
 - 13-14. (Canceled)
- 15. (Currently amended) The compound according to claim[[14]] 3, wherein each R attached to Y is independently selected from hydrogen or methyl.
 - 16-17. (Canceled)
- 18. (Previously presented) The compound according to claim 3, wherein Q_3 is substituted with 2 to 4 substituents, wherein at least one of said substituents is present in the ortho position relative to the point of attachment of Q_3 to the rest of the inhibitor.
- 19. (Original) The compound according to claim 18, wherein both ortho positions are occupied by one of said independently selected substituents.

- 20. (Original) The compound according to claim 19, wherein Q_3 is a monocyclic carbocyclic ring; and each of said ortho substituents on Q_3 are independently selected from halo or methyl.
- 21. (Previously presented) The compound according to claim 19, wherein Q_3 contains 1 to 2 substituents in addition to said ortho substituents, said additional substituents being independently selected from NR'_2 , OR', CO_2R' CN, $N(R')C(O)R^4$; $N(R')C(O)OR^4$; $N(R')S(O_2)R^4$; $N(R')R^4$; $N(R^4)_2$; OR^4 ; $OC(O)R^4$; $OP(O)_3H_2$; or $N=CH-N(R')_2$.
- 22. (Previously presented) The compound according to claim 3, wherein said compound is a compound of formula Ie:

$$O = \bigvee_{N=(A)_{\Pi}}^{R} \bigvee_{N=(A)_{\Pi}}^{R} X^{Q_{2}}$$

and is selected from any one of the following compounds:

cpd #	Structure	cpd #	Structure
208	CI NH2	209	CI ONH ₂

23. (Previously presented) The compound according to claim 3, wherein said compound is a compound of formula Ig:

$$O = \bigvee_{NH_2}^{R} \bigvee_{Q_2}^{R}$$

and is selected from any one of the following compounds:

cpd #	Structure	cpd #	Structure
302	CI ON NH ₂ OH	310	CI H ₂ N CO

Ttopij to	Office Action of May 23, 2006		
303	CI ONH2 H N CH3	311	E H
304	CI O NH ₂ NH	312	CI N H ₂ N CI
305		313	
306	CI O NH ₂	314	H ₃ C _S Cl

307	CI ON H ₂ OH	315	HO CI
308		316	CI N H ₂ N CI
319	F F CI CI CI CI	317	S H ₂ N CI
320	CI C	318	S H ₂ N CI
321	CI N H ₂ N O	328	H ₂ N CI

322	H ₂ N O CI	329	F CI
323	CI N H ₂ N O	330	F C C
324	CI O H ₂ N CI CH ₃	331	H ₃ C CI
325	CI CI H ₂ N O CI	332	F CH ₃ F CI
326	CI CI CI CI	333	F CI

	, , ,		
327	CI C	334	H ₃ C S H ₂ N O CI
337		335	CH ₃ H ₂ N O
338	F C O	336	
339	S H ₂ N CI	346	CI H ₂ N O CI
340	F C O	347	S H ₂ N CI
341	L Z Z Z Z C	348	F CI CI CI

	of May 23, 2000		
342	H ₂ N CI	349	CI N NH ₂
343	H ₂ N CI	350	CI NH ₂ N
344	F CI	351	CI ONH2 H OH
345	O H ₂ N O CI	352	CI O NH ₂ CH ₃

355	CI NH ₂	353	CI ONH2 FFF
356		354	
357	CI ON NH2	364	H ₂ N CI O NH ₂ CH ₃
358	CI ONH2 H	365	CI ONH ₂

359	CI NH ₂ H NH ₂	366	F O NH ₂
360	CI ONH ₂ H OH OH	367	P CH S CH S
361	NH ₂ CI NH ₃ F	368	F O NH ₂
362	NH ₂	369	F O NH ₂ CH ₃

	of May 23, 2000		
363		370	
373	CI NH ₂	371	F O NH ₂
374	CI ON SHAPE F	372	CI ONH2
375		382	

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376	CI ONH ₂ CH ₃ CH ₃	383	CI O NH ₂
377	CI ONH ₂ CH ₃	385	CI NH2 CH3
378	CI ONH2 OH	386	CI NH ₂ OH
379	NH ₂	387	CI NH2 FFFF

	of May 23, 2000		
380		388	
381	CH ₃ O NH ₂	389	CI O CH ₃
391	CI ONH ₂ F F	390	CI OH OH
392	CI ONH ₂ CI	396	CI ON H ₂

393	CI O CH ₃ O CH ₃	397	ONH ₂
394	CI ONH ₂ OH	398	CI ONH ₂ CI
395	CI ON H2 CH3	399	CI ON F
		1301	CI ONH ₂ CH ₃ CI

24. (Canceled)

25. (Previously presented) A pharmaceutical composition comprising an

amount of a compound according to claim 3 effective to inhibit p38, and a pharmaceutically

acceptable carrier.

26. (Previously presented) A method of treating inflammatory diseases,

destructive bone disorders, reperfusion/ischemia in stroke, myocardial ischemia, renal

ischemia, cardiac hypertrophy, rheumatoid arthritis, inflammatory bowel disease, ulcerative

colitis, or Crohn's disease in a patient, said method comprising administering to said patient a

composition according to claim 25.

27. (Previously presented) The method according to claim 26, wherein said

method is used to treat an inflammatory disease selected from acute pancreatitis, chronic

pancreatitis, asthma, allergies, or adult respiratory distress syndrome.

28. (Previously presented) The method according to claim 26, wherein said

method is used to treat rheumatoid arthritis, inflammatory bowel disease, ulcerative colitis, or

Crohn's disease.

29. (Previously presented) The method according to claim 26, wherein said

method is used to treat a destructive bone disorder selected from osteoarthritis, osteoporosis or

multiple myeloma-related bone disorder.

30-33. (Canceled)

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34. (Previously presented) The method according to claim 26, wherein said method is used to treat ischemia/reperfusion in stroke, myocardial ischemia, or renal ischemia.

35-37. (Canceled)